Amendments to the Claims

Please amend Claims 1, 4, and 20 as shown below. Please cancel Claims 25-27 and 31. This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

1. (Currently Amended) A method for detecting and quantifying clustered damages in DNA, the method comprising:

a) providing a sample containing DNA to be assayed for clustered damages;

b) contacting a first aliquot of the DNA to be tested for clustered damages with one or more lesion-specific cleaving reagents under conditions appropriate for cleavage of the DNA to produce single-strand nicks in the DNA at sites of damage lesions;

c) quantitatively determining the number average molecular length (L_n) of double stranded DNA in the lesion-specific cleaving reagent-treated first aliquot;

d) quantitatively determining the number average molecular length (L_n) of double stranded DNA in a second aliquot of the DNA to be tested for clustered damages, the second aliquot being untreated by lesion-specific cleaving reagents;

e) calculating the frequency of clustered damages ~~(-e)~~ (Φ_C) in the DNA to be assayed for clustered damages using the following equation:

$$\Phi_C = 1/L_n(+\text{enzyme}) - 1/L_n(-\text{enzyme})$$

wherein L_n(+enzyme) is the number average molecular length of double stranded DNA determined for the lesion-specific cleaving reagent-treated DNA determined in step c), and L_n(-

enzyme) is the number average molecular length of double stranded DNA determined for the untreated DNA in step d).

2. (Original) The method of Claim 1 wherein the DNA sample is obtained from a biological organism.

3. (Original) The method of Claim 1 wherein the DNA is genomic DNA.

4. (Currently Amended) The method of Claim 1 wherein the number average molecular length of double stranded DNA is determined by:

~~a)~~i) size fractionation of the DNA in an aliquot using non-denaturing gel electrophoresis; and

~~b)~~ii) quantitative electronic imaging of the fractionated DNA produced in step ~~a)~~i).

5. (Original) The method of Claim 1 wherein the lesion-specific cleaving reagent is a chemical reagent capable of cleaving the phosphodiester bond of the DNA molecule at abasic sites.

6. (Original) The method of Claim 1 wherein the lesion-specific cleaving reagent comprises lesion-specific enzymes.

7. (Original) The method of Claim 6 wherein the lesion-specific enzymes comprise:

a) a DNA glycosylase capable of cleaving the N-glycosyl bond of damaged nucleotides in a DNA molecule; and

b) a DNA endonuclease capable of cleaving the phosphodiester bonds of the DNA molecule at abasic sites produced by the DNA glycosylase.

8. (Original) The method of Claim 6 wherein the lesion-specific enzymes comprise one or more enzymes capable of cleaving the phosphodiester bond of a DNA molecule at abasic sites.

9. (Original) The method of Claim 7 or 8 wherein the lesion-specific enzyme capable of cleaving the phosphodiester bond of a DNA molecule at abasic sites is *E. coli* Nfo protein.

10. (Original) The method of Claim 6 wherein the lesion-specific enzymes comprise enzymes capable of cleaving the N-glycosyl bond of damaged nucleotides in a DNA molecule and cleaving the phosphodiester bonds at the site of the damaged nucleotide.

11. (Original) The method of Claim 10 wherein the lesion-specific enzymes comprise an enzyme which recognizes and cleaves DNA at sites of oxidized purines.

12. (Original) The method of Claim 11 wherein the enzyme is *E. coli* formamidopyrimidine-DNA glycosylase.

13. (Original) The method of Claim 10 wherein the lesion-specific enzymes comprise an enzyme which recognizes and cleaves DNA at sites of oxidized pyrimidines.

14. (Original) The method of Claim 13 wherein the enzyme is *E. coli* Nth protein.

15. (Original) The method of Claim 6 wherein the lesion-specific enzymes comprises:

a) Fpg protein; and

b) endonuclease III.

16. (Original) The method of Claim 6 wherein the lesion-specific enzymes comprises:

a) Fpg protein; and

b) endonuclease IV.

17. (Original) The method of Claim 6 wherein the lesion-specific enzymes comprises:

a) endonuclease III; and

b) endonuclease IV.

18. (Original) The method of Claim 6 wherein the lesion-specific enzymes comprises:

a) endonuclease III;

b) endonuclease IV; and

c) Fpg protein.

19. (Original) A method for detecting and quantifying clustered damages in DNA of a biological organism induced by exposure of the biological organism to a DNA-damaging agent, the method comprising:

a) providing a first sample of DNA obtained from the biological organism prior to exposure to a DNA-damaging agent, and a second sample of DNA obtained from the biological organism after exposure to a DNA damaging agent;

b) assaying each sample for clustered damages in the DNA by performing steps b) through e) of Claim 1 on each sample; and

c) subtracting the frequency of clustered damages (Φ_C) determined for the first sample, from the frequency of clustered damages determined for the second sample, to produce a value representative of the clustered DNA damage induced by exposure of the biological organism to the DNA-damaging agent.

20. (Currently Amended) The method of Claim 19 wherein the number average molecular length of double stranded DNA is determined by:

~~a)~~i) size fractionation of the DNA in an aliquot using non-denaturing gel electrophoresis; and

~~b)~~ii) quantitative electronic imaging of the fractionated DNA produced in step ~~a)~~i).

21. (Original) The method of Claim 19 wherein the DNA-damaging agent is X-rays.

22. (Original) The method of Claim 19 wherein the DNA-damaging agent is γ -rays.

23. (Original) The method of Claim 19 wherein the DNA-damaging agent is radon.

24. (Original) The method of Claim 19 wherein the DNA-damaging agent is a known carcinogen.

25. (Cancelled)

26. (Cancelled)

27. (Cancelled)

28. (Original) A method for detecting an accumulation of clustered damages in DNA of a biological organism, the method comprising determining the frequency of clustered damages in each DNA sample in a plurality of DNA samples obtained from a biological organism over a specified period of time by the method of Claim 1, and comparing the determined frequencies to one another to detect an accumulation of clustered damages in the biological organism over the period of time.

29. (Original) The method of Claim 28 wherein the biological organism is exposed to one or more DNA damaging agents over the period of time.

30. (Original) The method of Claim 29 wherein the DNA damaging agent is ionizing radiation.

31. (Cancelled)